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MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations
- of inventorship (Rule 4.17(iv)) for US only

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(54) Title: SOMATOSTATIN-DOPAMINE CHIMERIC ANALOGS

(57) Abstract: The invention features somatostatin-dopamine chimeric analogs and methods relating to their therapeutic use for the treatment of neoplasia, acromegaly, and other conditions.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/10891

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61K 38/00; C07K 2/00  
US CL : 514/2; 530/300

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 514/2; 530/300

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAVEANU, A. Clin. Endocrin. Metab. 2002, Vol. 87, No. 12, pages 5545-5552, Abstract, Title, and throughout.	1

<input type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

11 April 2005 (11.04.2005)

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/10891

### Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-18 and 20-102
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest



The additional search fees were accompanied by the applicant's protest.



No protest accompanied the payment of additional search fees.

**BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-18 and 20-102, drawn to Dop conjugates and methods of use.

Group II, claim(s) 19, drawn to compounds of formulae 3, 6, 11, 14, 18, 21, 24, and 27.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when the shared or corresponding technical feature is a contribution over the prior art. The inventions listed as Groups I-VII do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. The technical feature of Group I is the chimeric dopamine-somatostatin compound, which is shown by Saveanu (A Saveanu, et al, J. Clin. Endocrin. Metab. (2002) 87, 5545-5552) to lack novelty and inventive step and does not make a contribution over the prior art. Saveanu teaches a chimeric somatostatin-dopamine molecule, BIM-23A387 (Title, Abstract, throughout).

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

- 1) Dop1,2,or 3 conjugates with formula (I);
- 2) Dop 4 conjugates with formula (II);
- 3) Dop5 conjugates with formula (III);
- 4) Dop6 conjugates with formula (IV);
- 5) Dop7 conjugates with formula (V);
- 6) Dop8 conjugates with formula (VI);
- 7) Dop9 conjugates with formula (VII);
- 8) Dop10, or 11 conjugates with formula (VIII);
- 9) Dop12 conjugates with formula (IX); and
- 10) Dop13 conjugates with formula (X).

The claims are deemed to correspond to the species listed above in the following manner:

- 1) claims 2, 12-18, and 20-102;
- 2) claims 3, 12, 13, 20, 21, 27, 28, 34, 35, 41, 42, and 48-102;
- 3) claims 4, 12, 13, 20, 21, 27, 28, 34, 35, 41, 42, and 48-102;
- 4) claims 5, 12, 20, 27, 34, 41, and 48-102;
- 5) claims 6, 12, 20, 27, 34, 41, and 48-102;
- ~~6) claims 7, 12, 20, 27, 34, 41, and 48-102;~~
- ~~7) claims 8, 12, 20, 27, 34, 41, and 48-102;~~

## INTERNATIONAL SEARCH REPORT

International application N°.  
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- 8) claims 9, 12, 20, 27, 34, 41, and 48-102;
- 9) claims 10, 12, 20, 27, 34, 41, and 48-102;
- 10) claims 11, 12, 20, 27, 34, 41, and 48-102.

The following claim(s) are generic: claim 1 is generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: As stated above, a species of the broad generic claim 1 is taught by Saveanu. Further, according to PCT Rule 13.2 and the guidelines in Section (f)(i)(B)(1) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common structure. Although the chemical compounds of Claims 2-11 share a common property of being dopamine and/or somatostatin agonists, the compounds are not regarded as being of similar nature because all of the alternatives do not share a common structure, and are not an art recognized class of compounds. Each of the groups recites distinct somatostatin agonists which are linked to distinct dopamine agonists, and the chimeric compounds are not a recognized class of compound in the art, therefore the species lack unity of invention.

### Continuation of B. FIELDS SEARCHED Item 3:

STN registry structures of formula (I)-(X); caplus somatostatin, dopamine, conjugate, chimera;  
USPatents, USPGPUB, EPO, JPO, DERWENT dopamine somatostatin conjugate, chimera